

CLAIMS

1. An isolated polypeptide that specifically binds to a neoplastic cell or a cell of a pre-cancerous lesion, but does not specifically bind to a normal cell, wherein said
5 isolated polypeptide comprises amino acids 28-32, 51-53, and 90-100 of the sequence of SEQ ID NO:27, and wherein said normal cell is not a cell of the glomerular, fascicular zone of the adrenal gland or an epithelial cell of the collection tubes of the kidney.

- 10 2. The isolated polypeptide of claim 1, wherein said polypeptide further comprises amino acids 11-18, 36-43, and 82-104 of the sequence of SEQ ID NO:26.

- 15 3. An isolated polypeptide that specifically binds to a neoplastic cell or a cell of a pre-cancerous lesion, but does not specifically bind to a normal cell, wherein said isolated polypeptide comprises amino acids 11-15, 30-46, and 79-88 of the sequence of SEQ ID NO:2, but does not comprise the full-length sequence of SEQ ID NO:2, and wherein said normal cell is not a cell of the glomerular, fascicular zone of the adrenal gland or an epithelial cell of the collection tubes of the kidney.

- 20 4. The isolated polypeptide of claim 3, wherein said polypeptide further comprises amino acids 17-32, 48-54, and 87-95 of the sequence of SEQ ID NO:4, but does not comprise the full-length sequence of SEQ ID NO:4.

- 25 5. The isolated polypeptide of claim 1 or 3, wherein said polypeptide is capable of inducing apoptosis of said neoplastic cell or said cell of said pre-cancerous lesion, but does not induce apoptosis of said normal cell.

- 30 6. The isolated polypeptide of claim 1 or 3, wherein said neoplastic cell is selected from the group consisting of Barrett's tumors and tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and uterus.

7. The isolated polypeptide of claim 1 or 3, wherein said pre-cancerous lesion is selected from the group consisting of dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria *Helicobacter pylori*, tubular and tubulovillous adenomas of the
5 stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast
10 ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS).

8. The isolated polypeptide of claim 1 or 3, wherein said polypeptide is a functional fragment of an antibody selected from the group consisting of V_L, V_H, F_v, F_C, Fab, Fab', and F(ab')₂.

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9. The isolated polypeptide of claim 1 or 3, wherein said polypeptide specifically binds to a polypeptide comprising the sequence of SEQ ID NO:6.

10. An isolated nucleic acid molecule comprising nucleic acids 31-54, 106-
20 129, and 244-312 of the sequence of SEQ ID NO:28, and/or 82-96, 151-159, and or 268-300 of the sequence of SEQ ID NO:29.

11. An isolated nucleic acid molecule comprising nucleic acids 31-45, 88-138, and 235-264 of the sequence of SEQ ID NO:1, and/or nucleic acids 49-96, 142-162,
25 and 259-285 of the sequence of SEQ ID NO:3, wherein said nucleic acid molecule does not comprise the full-length sequence of SEQ ID NO:1 or SEQ ID NO:3.

12. An isolated nucleic acid molecule comprising the sequence of SEQ ID
NO:5.
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13. A vector comprising the nucleic acid sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:28, or SEQ ID NO:29.

14. An isolated cell comprising the vector of claim 13.

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15. An isolated cell that expresses the polypeptide of claim 1 or 3.

16. The isolated cell of claim 15, wherein said isolated cell is a mammalian cell.

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17. The isolated cell of claim 16, wherein said mammalian cell is a human cell.

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18. A method of producing the purified polypeptide of claim 1, said method comprising contacting a cell with a vector comprising SEQ ID NO:29 and isolating the polypeptide expressed by said vector.

19. The method of claim 18, wherein said vector further comprises the sequence of SEQ ID NO:28.

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20. A method of diagnosing a neoplasm or a pre-cancerous lesion in a mammal, said method comprising the steps of, (a) contacting a cell or tissue sample derived from said mammal with the purified polypeptide of claim 1 or 3, and (b) detecting whether said purified polypeptide specifically binds to said cell or tissue sample, wherein specific binding of said purified polypeptide to said cell or tissue sample is indicative of said mammal having a neoplasm or pre-cancerous lesion.

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21. The method of claim 20, wherein said cell or tissue sample is derived from a tissue selected from the group consisting of Barrett's tumors, tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and uterus, dysplasia of the gastric mucosa,
5 interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria *Helicobacter pylori*, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical
10 intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS).
- 15 22. The method of claim 20, wherein said polypeptide is conjugated to a detectable agent selected from the group consisting of a radionuclide, a fluorescent marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.
- 20 23. The method of claim 22, wherein said detectable agent is capable of inducing apoptosis of said cell.
24. The method of claim 20, wherein said polypeptide is conjugated to a protein purification tag.
- 25 25. The method of claim 24, wherein said protein purification tag is cleavable.
26. The method of claim 20, wherein said mammal is a human.
27. The method of claim 20, wherein said polypeptide is an antibody.

28. The method of claim 27, wherein said polypeptide is murine antibody
58/47-69.

29. A method of treating a proliferative disorder in a mammal, said method
5 comprising the step of contacting a cell with the purified polypeptide of claim 1 or 3,
wherein binding of said purified polypeptide to said cell results in the induction of
apoptosis of said cell.

30. The method of claim 29, wherein said mammal is a human.
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31. The method of claim 29, wherein said polypeptide is an antibody.

32. The method of claim 31, wherein said antibody is murine antibody 58/47-

15 33. The method of claim 31, wherein said antibody is a humanized antibody.

34. The method of claim 29, wherein said polypeptide is conjugated to a
detectable agent selected from the group consisting of a radionuclide, a fluorescent
marker, an enzyme, a cytotoxin, a cytokine, and a growth inhibitor.
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35. The method of claim 34, wherein said polypeptide is conjugated to a
protein purification tag.

36. The method of claim 35, wherein said protein purification tag is cleavable.
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37. A pharmaceutical composition comprising the isolated polypeptide of
claim 1 in a pharmaceutically acceptable carrier.

38. A diagnostic agent comprising the isolated polypeptide of claim 1 or 3.
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39. An isolated polypeptide, wherein said polypeptide comprises an amino acid sequence consisting of amino acids 469-518 of SEQ ID NO:6 or amino acids 5 739-748 of SEQ ID NO:6, and wherein said polypeptide does not comprise the full-length sequence of SEQ ID NO:6.

40. The isolated polypeptide of claim 39, wherein said polypeptide comprises an amino acid sequence consisting of amino acids 469-518 of SEQ ID NO:6.

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41. The isolated polypeptide of claim 39, wherein said polypeptide comprises an amino acid sequence consisting of amino acids 739-748 of SEQ ID NO:6.

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42. The isolated polypeptide of claim 39, wherein said polypeptide is at least

95% pure.

43. The isolated polypeptide of claim 39, wherein said polypeptide is specifically bound by murine antibody 58/47-69.

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44. The isolated polypeptide of claim 39, wherein said polypeptide comprises a tumor-specific glycostructure.

45. The isolated polypeptide of claim 39, wherein said polypeptide is expressed by a pre-cancerous lesion selected from the group consisting of dysplasia of the gastric mucosa, interstitial metaplasia of the stomach, inflammation of the gastric mucosa which is associated with the bacteria *Helicobacter pylori*, tubular and tubulovillous adenomas of the stomach, tubular adenoma of the colon, villous adenoma of the colon, dysplasia in ulcerative colitis, Barrett's dysplasia, Barrett's metaplasia of the esophagus, cervical intraepithelial neoplasia I, cervical intraepithelial neoplasia II, cervical intraepithelial neoplasia III, squamous epithelial metaplasia, squamous epithelial dysplasia of the bronchus, low grade and high grade prostate intraepithelial neoplasia (PIN), breast ductal carcinoma in situ (D-CIS), and breast lobular carcinoma in situ (L-CIS), and not by normal cells of the same tissue type.

15 46. The isolated polypeptide of claim 39, wherein said polypeptide is expressed by a tumor selected from the group consisting of Barrett's tumors and tumors of the esophagus, stomach, intestine, rectum, liver, gallbladder, pancreas, lungs, bronchi, breast, cervix, prostate, heart, ovary, and uterus, and not by a normal cell of the same tissue type.

20 47. A diagnostic agent comprising the isolated polypeptide of claim 39.

48. A method of inducing a tumor-specific immune response in a mammal, said method comprising the step of contacting said mammal with an isolated polypeptide comprising the sequence of SEQ ID NO:6, or a fragment comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, wherein said contacting induces a tumor-specific immune response in said mammal.

30 49. The method of claim 48, wherein said tumor-specific immune response comprises the production of an antibody that induces apoptosis of a cell which is specifically bound by said antibody.

50. The method of claim 48, wherein said fragment comprises amino acids 469-518 of SEQ ID NO:6 and amino acids 739-748 of SEQ ID NO:6 and does not comprise the full-length sequence of SEQ ID NO:6.

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51. A method of producing an isolated polypeptide comprising the sequence of SEQ ID NO:6 or a fragment thereof comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, said method comprising the steps of
10 (a) contacting a cell with a vector comprising a nucleic acid sequence that is substantially identical to SEQ ID NO:5 and (b) isolating the polypeptide expressed by said cell.

52. A method of identifying a candidate therapeutic compound, said method comprising the steps of (a) contacting a cell expressing a polypeptide comprising the 15 amino acid sequence of SEQ ID NO:6, or a fragment thereof comprising amino acids 469-518 of SEQ ID NO:6 or amino acids 739-748 of SEQ ID NO:6, with a test compound and (b) determining whether said test compound induces apoptosis of said cell and not of a control cell contacted with said test compound, wherein a test compound that induces apoptosis of said cell and not of said control cell is a candidate 20 therapeutic compound.

53. The method of claim 52, wherein said fragment comprises amino acids 469-518 of SEQ ID NO:6 and amino acids 739-748 of SEQ ID NO:6 and does not comprise the full-length sequence of SEQ ID NO:6.

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54. The method of claim 52, wherein said cell is adenocarcinoma cell line 23132 (DSMZ Accession No. DSM ACC 201).

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55. A method of producing an antibody that specifically binds to a neoplastic cell, said method comprising (a) administering the purified polypeptide of claim 39 to a mammal and (b) isolating from said mammal, an antibody that specifically binds to said polypeptide.

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56. The method of claim 55, wherein said polypeptide is purified from adenocarcinoma cell line 23132 (DSMZ Accession No. DSM ACC 201).

57. The method of claim 55, wherein said method further comprises isolating
10 a cell expressing said antibody from said mammal.